

Session Goals and NIMH Research Priorities in CNS and Myeloid Reservoirs

Jeymohan Joseph, PhD

Division of AIDS Research

National Institute of Mental Health

NIMH Satellite Symposium: Leveraging Host Cellular Pathways for Targeting HIV CNS/Myeloid Reservoirs

11th Edition, HIV Persistence During Therapy Meeting,
Ft. Lauderdale, FL

December 10, 2024



National Institute
of Mental Health

Leveraging Host Cellular Pathways for Targeting HIV CNS/Myeloid Reservoirs

CONFLICT OF INTEREST

NONE

Leveraging Host Cellular Pathways for Targeting HIV CNS/Myeloid Reservoirs

GOALS

The Goal is this session is to highlight studies focused on understanding the role of host signaling pathways and cell death (apoptosis, autophagy) in regulating mechanisms of HIV reservoir persistence and strategies to target them in CNS derived cells (macrophage, microglia, pericytes)

Leveraging Host Cellular Pathways for Targeting HIV CNS/Myeloid Reservoirs

Metabolic strategies to eliminate CNS Myeloid Viral Reservoir

Eliseo Eugenin, University of Texas, Galveston, TX

Strategies for Depletion of HIV reservoir by activation of ISR Signaling

Guochun Jiang, University of North Carolina, Chapel Hill, NC

Targeting HIV Myeloid Reservoirs in the CNS by IAP and TREM1 Inhibition

Grant Campbell, University of South Dakota, Vermillion, SD

Leveraging Host Cellular Pathways for Targeting HIV CNS/Myeloid Reservoirs

Targeting the HIV-1 Reservoir in Myeloid Cells using the SECH approach

Jin Wang, Methodist Hospital Research Institute, Houston, TX

Modulation of HIV Reservoir Dynamics in Brain Pericytes

Michal Toborek, University of Miami School of Medicine, Miami, FL

Repurposing BCL-2 and Jak 1/2 inhibitors for targeting myeloid reservoirs

Boghuma Kabisen Titanji, Emory University, Atlanta, GA

Leveraging Host Cellular Pathways for Targeting HIV CNS/Myeloid Reservoirs

Research Gaps and Future Research Areas Discussion

Co-Chairs: Mario Stevenson, University of Miami, Miami, FL

Kiera Clayton, University of Massachusetts, Worcester, MA

Leveraging Host Cellular Pathways for Targeting HIV CNS/Myeloid Reservoirs

Role of Myeloid Cells in Persistence and Eradication of HIV-1 Reservoirs from the Brain (R01)

RFA-MH-18-300

RFA-MH-20-701

National Institute of Mental Health ([NIMH](#))

National Institute on Drug Abuse ([NIDA](#))

National Institute of Neurological Disorders and Stroke ([NINDS](#))

Eradication of HIV-1 from CNS/Myeloid Reservoirs

Identify and characterize persistent/latent HIV in cells derived from the central nervous system

Mechanisms involved in the temporal establishment, maintenance, and resurgence of persistent/latent HIV in the CNS

Physiologically relevant animal models and CNS-based cellular assays that recapitulate HIV persistence and latency in CNS

Assess CNS toxicity and adverse impact of current and emerging eradication strategies

Discover novel imaging approaches and cellular biomarkers to detect latently/ persistently infected cells in the CNS

Funding Announcements

Role of T-Cells in HIV CNS Reservoir Seeding, Persistence, and Neuropathogenesis (R01 Clinical Trial Not Allowed)

RFA-MH-26-110/111

Application Receipt date: March 18, 2025

The goal of this NOFO is to encourage research to define the mechanisms and roles of T-cells in HIV/CNS (central nervous system) reservoir seeding, persistence and neuropathogenesis. Strategies to develop therapeutic approaches to target T-cell neuro-invasion, reservoir maintenance, and neuropathogenesis is also an area of high priority. State-of-the-art CNS cell systems, organoid models, post-mortem tissue, animal models, clinical samples and single-cell technologies can be used as potential tools to address this research area.

Current DAR Notices of Special Interest (NOSIs) in NeuroHIV

Notice of Special Interest (NOSI): Eradication of HIV-1 from Central Nervous System Reservoirs

Notice Number:

NOT-MH-23-260

Notice of Special Interest (NOSI): Clinical Studies of CNS Complications in People with HIV

Notice Number:

NOT-MH-23-255

Notice of Special Interest (NOSI): Neuropathogenesis of CNS Complications Associated with HIV

Notice Number:

NOT-MH-23-280

For a full list of the Division's NOSIs please go to:

<https://www.nimh.nih.gov/about/organization/dar/aids-related-funding-opportunity-announcements>

Current DAR Notices on HIV Cure-Related Research

- **NOSI**

Notice of Special Interest (NOSI): HIV Cure-Related Research in Diverse Populations

Notice Number:

NOT-AI-23-046

Funding Opportunity Title

Opportunities for HIV Cure Strategies at the Time of ART Initiation
(R01 Clinical Trial Not Allowed)

Activity Code

R01 Research Project Grant

For a full list of the Division's funding opportunities please go to:

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National NeuroHIV Tissue Consortium



3,378 participants to date

3 clinical sites, 5 tissue bank sites

1,145 brains and other organs from PWH, 344 from PWoH.

1722 PWH and 78 PWoH have been followed longitudinally with detailed medical, neuropsychological/neuro cognitive, and psychiatric assessments

Also includes data and biofluids from CHARTER studies

981 requests with shipments of 27,251 cases (often more than one sample per case), resulting in 798 publications to date

- 80 brains (and other organs) from virally-suppressed PWH
- Currently over 110 virally-suppressed PWH followed longitudinally
- Fresh-frozen and formalin-fixed tissue available along with detailed clinical data

- **Key Publications about HIV reservoirs and persistence**
 - **Gabuzda D et al.** Intact Proviral DNA Analysis of the Brain Viral Reservoir and Relationship to Neuroinflammation in People with HIV on Suppressive Antiretroviral Therapy. *Viruses*. 2023
 - **Oliveira MF et al.** Evaluation of Archival HIV DNA in Brain and Lymphoid Tissues. *J Virol*. 2023.
 - **Angelovich TA et al.** Regional Analysis of Intact and Defective HIV Proviruses in the Brain of Viremic and Virally Suppressed People with HIV. *Ann Neurol*. 2023
 - **Cochrane CR et al.** Intact HIV Proviruses Persist in the Brain Despite Viral Suppression with ART. *Ann Neurol*. 2022
 - **Ko A et al.** Macrophages but not Astrocytes Harbor HIV DNA in the Brains of HIV-1-Infected Aviremic Individuals on Suppressive Antiretroviral Therapy. *J Neuroimmune Pharmacol*. 2019

Division of AIDS Research, NIMH

Thank
You!

Contacts:

Dianne Rausch, Division Director

drausch@nih.gov

Jeymohan Joseph, NeuroHIV Branch Chief

jjeymoha@nih.gov

Vasudev Rao, NeuroHIV Program Official

vasudev.rao@nih.gov

Beth Finch, NNTC Program official

beth.finch@nih.gov